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SCIENCE

The five members of the United States Atomic Energy Commission in session at their new offices in Washington 26 November. Robert F. Bacher, 41-year-old Cornell physicist, youngest member, and only scientist on the Commission appointed 28 October, is seated on the extreme right. (See *Science* 8 November.) Chairman David E. Lilienthal, who resigned as chairman of TVA to accept the new post, is seated next to Dr. Bacher. Standing from left to right are William W. Waymack, a former Pulitzer Prize winner in editorial writing; Lewis L. Strauss, partner in Kuhn, Loeb & Company, bankers; and Sumner L. Pike, former member of the Securities and Exchange Commission.

New Horizons in Medical Research

C. J. Van Slyke

Science

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SCIENCE

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New Horizons in Medical Research

C. J. Van Slyke

Medical Director, U. S. Public Health Service, and *Chief, Research Grants Division*
National Institute of Health, Bethesda, Maryland

A LARGE-SCALE, NATIONWIDE, peacetime program of support for scientific research in medical and related fields, guided by more than 250 leading scientists in 21 principal areas of medical research, is now a functioning reality. The program, based on U. S. Public Health Service Research Grants financed by public funds, supports research—conducted without governmental control—by independent scientists. The purpose of these grants is to stimulate research in medical and allied fields by making available funds for such research and by actively encouraging scientific investigation of specific problems on which scientists agree that urgently needed information is lacking. Accompanying this purpose is complete acceptance of a basic tenet of the philosophy upon which the scientific method rests: The integrity and independence of the research worker and his freedom from control, direction, regimentation, and outside interference.

The U. S. Public Health Service Research Grants, in operation as a medical research program of scientists and by scientists, may have early and profound effects upon the course of medical history and the national health.

The program, both in principle and as administered, has been welcomed and approved wholeheartedly by leaders in medical research. A total of 264 research projects, supported by $3,900,000 granted from the inception of the program late in 1945 up to 15 October 1946, already have been undertaken in 77 universities, hospitals, and other public and private institutions in 26 states. Although the program is less than a year old and has been little publicized, interest is rapidly widening, and new applications already are being received at a rate greater than 800 per year.

It is obvious that enormous savings of public and private money would result from research leading to wholesale prevention or cure of cancer, tuberculosis, diabetes, chronic nephritis, pernicious anemia, mental disorders, the common cold, heart diseases, and other widespread ailments.

Medical research costs money, however, and in the past a large amount of potentially very important research has not been conducted because funds have not been available to pay for it. Many universities and other nonprofit institutions have extremely limited funds for research, even though their teaching staffs, graduate students, and other personnel have the talent, training, and interest necessary for scientific investigation. Although research conducted by industrial organizations does add considerably to the total fund of medical knowledge, such research quite often must be directed toward specific goals.

The great benefits from all medical research, wherever conducted, are received by the millions of people whose lives are made healthier, happier, and longer through widespread application of knowledge gained in research laboratories. Conversely, research not conducted for want of funds is very costly to the same millions. The essence of these facts, as related to the Research Grants program, has been stated by the National Health Advisory Council: "There are few purposes for which public funds could be used more appropriately than to discover ways to prevent and cure illness and to prolong useful years of life." The function of the Research Grants is to make it possible for workers in medical and allied sciences to expedite, extend, and intensify health-saving and life-saving research.

During the war it frequently was necessary to sacrifice fundamental, not immediately applicable research in order to arrive at specific objectives promptly; promising bypaths often had to be by-passed. In the normal course of scientific investigation, however, the bypaths quite often lead to more important findings than do the roads from which they branch. Much of the most important research may not appear immediately to lend itself to clinical application, but it builds a large body of information, assembled parts from which may later have wide clinical applicability. The necessity for immediately restocking and enlarging the storehouse of fundamental data which forms the basis on which further advances in the medical sciences can be made is widely recognized, and the

opportunity to do this, curtailed during the war, is now greatly broadened.

In addition to research findings of immediate or ultimate applicability to the causes, diagnosis, treatment, and prevention of disease, benefits to be expected include an unprecedented opportunity to expand the Nation's resources in the fields of medical research. New nuclei of research can develop in universities, colleges, and other institutions which, heretofore, for want of funds, have been unduly limited in conducting scientific investigation. This expansion of activities in the field of medical research will provide training and experience for many promising young scientists and thus will enlarge significantly the ranks of qualified research workers necessary to carry on independently investigations in this field in the future. This aspect of the Research Grants supplements and complements the National Institute of Health Research Fellowships, which are described more fully in subsequent paragraphs.

Research Grants funds are *"additive"* and, as such, are intended to provide support for *additional* research—research that would not be conducted if additional funds were not available. They are not *"substitutive"* and therefore are not to be used to relieve a university or other institution of its financial responsibilities for usual or normal teaching, administrative, or research functions. Research Grants funds, however, may compensate for loss of teaching time if a substitute is employed to relieve the research director of normal teaching or administrative responsibilities, although supplementation of existing salaries cannot be provided. Furthermore, not more than 8 per cent—allowed only when fully justified—of the total amount of any grant may be budgeted for "overhead." Thus, the "additive" use of Research Grant funds does not in any way alter the financial structure of a participating institution.

Authority for the Research Grants

The Congress, in enacting Public Law 410, known as the Public Health Service Act, in 1944, stated the general powers and duties of the Public Health Service with respect to research and investigations. The law states that:

"The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of the physical and mental diseases and impairments of man. . . ."

In carrying out the foregoing, the Surgeon General was authorized by the Congress in Public Law 410 and in amendments to "make grants in aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals" for such research projects as are recommended by the National Advisory Health Council, the National Advisory Cancer Council, and the National Advisory Mental Health Council.

National Advisory Councils

These three Advisory Councils have been designated by the Congress to make recommendations to the Surgeon General of the U. S. Public Health Service regarding means necessary or appropriate to carry out his responsibilities with respect to research and investigations.

One of the important functions of the Councils is to act upon applications for Research Grants, with the advice and recommendation of special Study Sections composed of groups of scientists in the major categories of medical research.

The National Advisory Health Council consists of 14 members, 10 of whom are outstanding civilian scientists. The other experts are the director of the National Institute of Health and one representative each from the Army, the Navy, and the Bureau of Animal Industry as ex-officio members of the Council. This Council makes recommendations regarding all Research Grants except those relating specifically to research in the fields of cancer and mental health. Membership on this Council is for a period of five years; two new members are appointed each year to replace two retiring members.

The National Advisory Cancer Council, which, in addition to the Surgeon General, who serves as chairman, ex-officio, consists of 6 members selected from among leading medical and scientific authorities who are outstanding in the study, diagnosis, and treatment of cancer, reviews applications for Grants for research projects which show promise of making valuable contributions to the cause, prevention, or methods of diagnosis or treatment of cancer. Membership is for a period of three years; two new members are appointed each year to replace retiring members.

The National Mental Health Council consists of 7 members, including the Surgeon General, who is ex-officio chairman, and 6 members appointed from among leading medical or scientific authorities outstanding in the study, diagnosis, and treatment of psychiatric disorders. This Council reviews all applications for Research Grants for studies relating to the cause, prevention, and treatment of mental diseases. Membership is for three years, and two new members appointed each year replace retiring members.

Special Study Sections

At the request of the three Advisory Councils the fields of medical research were classified into major categories by the Research Grants Division of the

National Institute of Health. Special Study Sections made up of consultant experts in more than 20 major categories have been set up to provide the Advisory Councils with the benefit of their advice and judgment in passing upon applications for Research Grants. Members of the Study Sections include many of the Nation's outstanding research workers in medical and related sciences.

The special Study Sections have two major responsibilities: (1) to review applications for Research Grants in their respective fields, approving them, suggesting changes or further study, or disapproving them, and forwarding their recommendations to the appropriate National Advisory Councils; and (2) as scientific leaders, to survey the status of research in their fields in order to discern neglected areas in which research is particularly wanting, and to stimulate the interest of workers competent to undertake needed research.

Most Study Sections include a representative of the Army, the Navy, the Veterans Administration, and the Public Health Service.

The member from the Public Health Service serves as the executive secretary of each Section. Conferences of executive secretaries concerned are conducted whenever there is any question as to which Study Section should consider a particular application for a grant. If these executive secretaries decide that an application concerns more than one Study Section, the application is referred to one Section, which may seek advice of other Sections. Most Study Sections have regular quarterly meetings a few weeks in advance of the quarterly meeting of the National Advisory Councils.

Each Study Section, consisting essentially of outstanding civilian scientists, constitutes a scientific group with full authority and responsibility to make expert recommendation as to whether a research project application is acceptable and can be supported by Research Grants funds.

Study Sections inform workers in their respective fields, through announcements in appropriate professional journals or other publications, of the availability of Research Grants funds and of such other information as will further research in their fields.

Research Grants Division
The National Institute of Health

The Research Grants Division of the National Institute of Health was established late in 1945 to administer the Research Grants program of the U. S. Public Health Service. This Division is the administrative agent of the U. S. Public Health Service in relation to the National Advisory Health Council, National Advisory Cancer Council, and the National Mental Health Council. Applications for grants for research projects to be considered by any one of these three Councils, therefore, should be made to the Research Grants Division. When there is any question as to which Council should consider an application, this is solved by a meeting of the executive secretaries of the Study Sections set up under the various Councils. The principal responsibility of the Division is to conduct all administrative procedures in connection with Research Grants and to assist the special Study Sections and the National Advisory Councils in furthering medical research.

In addition to correlating and centralizing, in one office, administration of all Research Grants programs in the various Institutes and Divisions of the Public Health Service, the Research Grants Division is currently setting up a clearinghouse of data concerning medical research conducted under grant-in-aid programs of government, public, and privately financed agencies.

Kinds of Research Which May Be Conducted

Research "relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man" falls within the scope of the Research Grants. Included is research in the fields of medicine, surgery, dentistry, antibiotics, bacteriology, biochemistry and nutrition, biophysics, cardiovascular diseases, endocrinology, gerontology, hematology, industrial diseases, malaria, pathology, pharmacology, physiology, public health methods, neurology, psychiatry, psychology, cancer, sanitation, venereal diseases, tropical diseases, virus and rickettsial diseases, and others.

In general, clinical work of a nonresearch character and nonmedical investigations in such fields as mathematics, physics, and chemistry are beyond the purposes of the program, although research projects in these fields may be conducted if they are considered likely to provide data applicable to medical science.

Whether a particular research proposal lies within these limits is determined by the appropriate special Study Section and National Advisory Council appraising the proposal.

Projects which are purely demonstrations of the application of epidemiologic, diagnostic, therapeutic, or preventive measures in the control of diseases do not qualify for Research Grants. (Aid for demonstration projects is provided by various divisions of the Public Health Service other than the Research Grants Division.)

A research project which has incidental demonstration aspects may be recommended for approval at the

discretion of the appropriate special Study Section and National Advisory Council.

Who May Apply for Research Grants

The Congress has authorized grants-in-aid for medical research to: universities, hospitals, laboratories, other public or private institutions, and individuals.

It is apparent that under the law no organization or individual is barred from applying for a grant-in-aid for research in a medical field. Although individuals may apply, the Research Grants Division encourages individual applicants to affiliate with a university, institution, laboratory, or other organization, since such affiliation greatly facilitates administration of grants, relieves the research worker of responsibility for bookkeeping and auditing, and provides him with better facilities than ordinarily would be available to an individual.

How Applications for Research Grants Are Made

Applications for grants-in-aid for medical research should be made on application forms available upon request from: Chief, Research Grants Division, National Institute of Health, Bethesda 14, Maryland.

Application forms provide for information regarding objectives of the proposed research, contemplated methods, and budget plan.

In order that administrative approval be indicated, an application made in the name of a university or other organization should be signed by an administrative official, such as the dean or president, rather than by the director of the project or departmental head.

The dean, department head, professor, or research director most familiar with the work of the applicant is requested to submit a letter giving his evaluation of the research proposal and of the investigator under whose immediate direction it is to be conducted.

The treasurer, bursar, or comptroller (by title) should be named as payee.

Applications may be submitted at any time, addressed to: Chief, Research Grants Division, National Institute of Health.

The Processing of Applications for Research Grants

Applications received by the Research Grants Division are reviewed by a special Study Section and a National Advisory Council.

Immediately upon receipt by the Division, each application for a grant-in-aid for medical research is duplicated, and a copy is forwarded promptly to each member of the special Study Section of experts in the field in which the proposed research lies. (Applications relating to research in the fields of cancer and mental health are forwarded by the Research Grants Division to the National Cancer Institute and the Mental Hygiene Division of the U. S. Public Health Service for submission to the appropriate Study Sections of the National Advisory Cancer Council and the National Advisory Mental Health Council.)

Each Study Section member, upon receiving an application forwarded to him, gives it preliminary consideration. If a Study Section member desires further information on a proposal, he may ask the Research Grants Division or the executive secretary of his Study Section to write the applicant, or, upon arrangement with the Study Section chairman, he personally may make direct inquiries or inspections.

At each regular or special meeting of a Study Section, all applications received since the previous meeting are formally considered without any priority ranking of research proposals.

Action by a special Study Section on a research proposal may consist of advising: (1) that it be accepted as submitted, (2) that it be rejected, or (3) that it be deferred pending further investigation or receipt of additional information. In advising any of these dispositions, Study Section members consider: (1) the scientific merits of the proposed research, (2) ability and training of investigator, (3) facilities available to investigator, and (4) such other considerations as the Section members regard as pertinent.

An application for a Research Grant is considered solely on the merits of the proposal; the applicant institution is not required to match any of the necessary funds requested.

After an application has been considered by a Study Section, it is forwarded with the Section's recommendation to the appropriate National Advisory Council for consideration at its next quarterly meeting. The advice of the Sections regarding applications usually is accepted by the Advisory Councils, but the latter are not obligated to accept this advice. If a Study Section disapproves an application, the Advisory Council, in all probability, will disapprove it also, and the applicant will be so advised. If the disapproving Study Section or Advisory Council indicates that a revision of the application might result in subsequent favorable action, the applicant is so informed.

All projects recommended by the Advisory Councils for approval are forwarded to the Surgeon General. After a research project has been approved by the Surgeon General, the applicant is notified and a check is sent to the payee. The research under an approved application may begin at any time in the year.

Since the Research Grants program is a peacetime program, emphasis is not placed on abnormal speed in conducting research. Research projects which will

take from three to five years or more may receive favorable consideration.

Grants of funds are made on a yearly basis; however, duration of the proposed investigation is an important consideration of the Study Sections and Advisory Councils in their decisions regarding recommendations for action. Approval of a project which the applicant has estimated will require more than a year to complete signifies a grant of funds for one year and an indication to the grantee of continued favorable action for as long as progress reports justify and Congress appropriates necessary funds. If a project requires more than one year to complete, a new application for continuation of the project must be submitted for each succeeding year; such renewal applications are processed in the same way as original applications.

An initially approved application is paid in full at the beginning of the first year. If an investigator needs additional funds during the year, he may file a supplementary application. If any funds remain unexpended at the end of a year, the amount given the investigator for the next year is adjusted. If any funds remain unexpended at the completion of a project, they are returned to the U. S. Government. Since any equipment or supplies purchased with Research Grants funds belong to the grantee rather than to the U. S. Government, no terminal accounting for such property is required.

How Research Is Conducted Under Research Grants

Research under the Research Grants program is conducted with full independence and autonomy of the research investigator. Support of research through the use of Research Grants funds does not imply in any way any degree of Federal control, supervision, or direction of the research project. The autonomy of the individual research worker implied in this philosophy, however, does not exclude self-imposed guidance entailed in the over-all plan of an organized, cooperative research project in which several groups of investigators may collaborate.

In order not to divert the time of the researcher unnecessarily from the actual conduct of the research investigation, only annual scientific progress reports are requested. It is not desired that the preparation of these reports present any long, tedious burden to the investigator, and it is therefore requested that they contain only such data in a brief, clear, and concise manner as will permit the appropriate Study Section and National Advisory Council to be adequately informed as to the conduct of the research investigations since the submission of the previous progress report. In this way the appropriate Study Section and National Advisory Council will be in a position to indorse the grant as it comes up for renewal annually. There may be certain instances in which a group of cooperative research investigators are concerned with a special problem of which interim reports are desired. These, however, are the exceptional instances.

Reports made to Study Sections are confidential and information from them is not circularized to other investigators without the consent of the grantee.

In order to avoid the possibility of restricting the autonomy of the research worker in any way, the Research Grants Division, the special Study Sections, and the National Advisory Councils will not review any papers proposed for publication, and therefore they are not in a position to indicate either approval or disapproval of such papers published solely at the election of, and under the complete control of, the research workers. This does not indicate any lack of interest in the results of research projects, but is aimed entirely at avoiding any degree of governmental restriction. After papers have been published, however, it is requested that the research workers provide the Research Grants Division with 50 reprints. It is also requested that published papers carry footnote acknowledgments of the Research Grant assistance from the Public Health Service.

Twice each year grantees submit simple financial reports to show current status of funds. The purpose of these reports is to facilitate routine auditing of Federal funds expended and to permit prompt re-granting of any funds which may remain unused at the expiration of yearly grants.

National Institute of Health Research Fellowships

In order to further the development and training of competent research workers in the medical sciences and related fields, the National Institute of Health Research Fellowships program was established in 1945 under authority granted by the Congress in the Public Health Service Act.

Although this program is not administered by the Research Grants Division, its purposes are closely related to those of the Research Grants program.

The National Institute of Health Research Fellowships are awarded to individuals who have had post-graduate work in institutions of recognized standing in the various fields of medical and related sciences, such as biology, chemistry, physics, entomology, public health, medicine, dentistry, veterinary medicine, and others.

Applications for these fellowships may be made at any time during the year, are acted upon promptly, and are effective for one year from the time of award,

with a possibility of renewal for a second year.

Junior research fellowships are available to individuals holding Master's degrees or to those who have completed an equivalent number of hours of post-graduate study. The stipend is $2,400 per annum.

Senior research fellowships are available to individuals holding doctorate degrees. The stipend is $3,000 per annum. At the present time plans are being effected for the granting of fellowships to individuals at the level of B.S. or A.B. degree. The stipend likely will approximate $1,800 per annum.

These fellowships offer opportunities for study and research in association with highly trained specialists in candidates' chosen fields either at the National Institute of Health or any other approved institutions of higher learning. Letters of inquiry regarding them should be addressed to: The Director, National Institute of Health, Bethesda 14, Maryland.

Summary

From the above it is seen that the U. S. Public Health Service Research Grants program represents a sincere and continuing effort to supply Federal funds for the support of necessary additional research in the fields of medical and related sciences without interposing any degree of government restriction, control, supervision, or regimentation. The program is a scientific one, scientific guidance of which lies wholly in the hands of scientists.

Membership of National Advisory Councils

National Advisory Health Council

Gordon M. Fair, Graduate School of Engineering, Harvard University, Cambridge 38, Massachusetts.

Edwin B. Fred, University of Wisconsin, Bascom Hall, Madison, Wisconsin.

A. Baird Hastings, Department of Biological Chemistry, Harvard Medical School, Boston 15, Massachusetts.

Carl S. Marvel, 213 Noyes Laboratory, University of Illinois, Urbana, Illinois.

Kenneth F. Maxcy, School of Hygiene & Public Health, The Johns Hopkins University, 615 N. Wolfe Street, Baltimore 5, Maryland.

Karl F. Meyer, Director, The George Williams Hooper Foundation for Medical Research, University of California Medical Center, San Francisco 22, California.

John H. Musser, 1430 Tulane Avenue, New Orleans 13, Louisiana.

Harry S. Mustard, Columbia University School of Public Health, 600 West 168th Street, New York 32, New York.

William C. Rose, Noyes Laboratory of Chemistry, University of Illinois, Urbana, Illinois.

Henry F. Vaughan, Dean, School of Public Health, University of Michigan, Ann Arbor, Michigan.

(*Ex-Officio Members*)

Capt. O. L. Burton (MC), USN, Chief, Preventive Medicine Division, Bureau of Medicine & Surgery, Potomac Annex, Navy Department, Washington 25, D. C.

Assistant Surgeon General R. E. Dyer, Director, National Institute of Health, U. S. Public Health Service, Washington 14, D. C.

Col. Karl R. Lundeberg (MC), Chief, Preventive Medicine Division, Office of The Surgeon General, U. S. Army, Washington 25, D. C.

Harry W. Schoening, Chief, Pathological Division, Bureau of Animal Industry, U. S. Department of Agriculture, Washington 25, D. C.

National Advisory Cancer Council

Robert S. Stone, University of California Medical School, San Francisco 22, California.

Charles B. Huggins, Department of Surgery, University of Chicago, Chicago 37, Illinois.

George M. Smith, Yale University Medical School, 333 Cedar Street, New Haven, Connecticut.

Sherwood Moore, Director, Mallinckrodt Institute of Radiology, Washington University, St. Louis, Missouri.

Frank E. Adair, Memorial Hospital for the Treatment of Cancer and Allied Diseases, York Avenue and 68th Street, New York, New York.

A. C. Ivy, Northwestern University Medical School, Ward Memorial Building, 303 E. Chicago Avenue, Chicago 11, Illinois.

National Advisory Mental Health Council

Edward A. Strecker, Department of Psychiatry, University of Pennsylvania, 111 North 49th Street, Philadelphia, Pennsylvania.

William C. Menninger, Medical Director, Menninger Clinic, Topeka, Kansas.

John Romano, Professor of Psychiatry, School of Medicine, University of Rochester, Rochester, New York.

Frank F. Tallman, Commissioner of Mental Diseases, State of Ohio, State Office Building, Columbus, Ohio.

George S. Stevenson, Medical Director, National Committee for Mental Hygiene, 1790 Broadway, New York, New York.

David M. Levy, 300 Park Avenue, New York, New York.

Membership of Study Sections[1]

I. *Antibiotics Study Section*

Hans T. Clarke, Columbia University, *Chairman*; C. J. Van Slyke, National Institute of Health, *Executive Secretary*; David P. Barr, Cornell University; Robert D. Coghill, Abbott Laboratories; Vincent du Vigneaud, Cornell University; Harry Eagle, Johns Hopkins School of Hygiene; R. P. Herwick, Food and Drug Administration; Colin MacLeod, New York University; E. K. Marshall, Jr., Johns Hopkins University; J. E. Moore, Medical Arts Building, Baltimore; W. H. Peterson, University of Wisconsin; Milton V. Veldee, U. S. Public Health Service; Henry Welch, Food and Drug Administration; Oskar Wintersteiner, Squibb Institute for Medical Research; W. Barry Wood, Jr., Washington University; Maj. Ed-

[1] Additional Study Sections are being formed, membership of which will be announced when complete.

ward H. Vogel, Jr., U. S. Army; Capt. George B. Dowling, U. S. Navy; Arthur M. Walker, Veterans Administration.

II. *Bacteriology Study Section*

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III. *Biochemistry and Nutrition Study Section*

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IV. *Cardiovascular Study Section*

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V. *Dental Study Section*

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VI. *Gastric Cancer Study Section*

George M. Smith, Yale University, *Chairman*; Alexander Brunschwig, University of Chicago; Mandred W. Comfort, Mayo Clinic; Andrew C. Ivy, University of Illinois; Sherwood Moore, Washington University; George T. Pack, Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York; Leonell C. Strong, Yale University; Owen H. Wangensteen, University of Minnesota; Shields Warren, New England Deaconess Hospital.

VII. *Gerontology Study Section*

Henry S. Simms, Columbia University, *Chairman*; Nathan W. Shock, National Institute of Health, *Executive Secretary*; Max A. Goldzieher, 104 East 40th Street, New York; Roy G. Hoskins, 25 Shattuck Street, Boston; Oscar J. Kaplan, San Diego State College; Clive M. McCay, Cornell University Agricultural Experiment Station; Wm. deB. MacNider, University of North Carolina; Robert A. Moore, Washington University School of Medicine; Capt. G. B. Tayloe (MC), U. S. Navy.

VIII. *Hematology Study Section*

Charles A. Doan, Ohio State University, *Chairman*; Kenneth M. Endicott, National Institute of Health, *Executive Secretary*; Edwin J. Cohn, Harvard Medical School; Henry N. Harkins, Johns Hopkins Hospital; Roy R. Kracke, University of Alabama Medical College; Carl V. Moore, Washington University School of Medicine; Joseph Stasney, Jefferson Medical College; M. M. Wintrobe, University of Utah; Col. William S. Stone, U. S. Army; Lt. Cdr. E. P. Cronkite, U. S. Navy; Francis P. Parker, Veterans Administration.

IX. *Malaria Study Section*

James A. Shannon, Squibb Institute for Medical Research, *Chairman*; G. Robert Coatney, National Institute of Health, *Executive Secretary*; G. A. Carden, Jr., New York City; L. T. Coggeshall, University of Chicago; A. C. Cope, Massachusetts Institute of Technology; Robert C. Elderfield, Columbia University; Clay G. Huff, University of Chicago; Robert F. Loeb, Columbia University; E. K. Marshall, Jr., Johns Hopkins University School of Medicine; Paul F. Russell, Rockefeller Foundation; Col. Karl R. Lundeberg, U. S. Army; Capt. James J. Sapero, U. S. Navy; E. A. Martin, Veterans Administration.

X. *Mental Health Study Section*

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stitute for Research, Cincinnati; Lucille Petry, U. S. Public Health Service; Marian C. Putnum, 37 Marlborough Street, Boston; David Rapaport, Menninger Clinic; Fritz Redl, Wayne University; George Richard Wendt, University of Rochester; Abner Wolf, Columbia University; Harold G. Wolff, Payne Whitney Psychiatric Clinic, New York; S. B. Wortis, Bellevue Hospital, New York.

XI. *Metabolism and Endocrinology Study Section*

Joseph H. Barach, University of Pittsburgh, *Chairman*; Hugh L. C. Wilkerson, Harvard School of Public Health, *Executive Secretary*; Jerome W. Conn, University of Michigan Medical School; Francis D. W. Lukens, University of Pennsylvania; Alexander Marble, 81 Bay State Road, Boston; Henry B. Mulholland, University of Virginia Hospital; Lester J. Palmer, The Mason Clinic, Seattle; Elaine P. Ralli, New York University College of Medicine; Henry T. Ricketts, University of Chicago; Randall G. Sprague, Mayo Clinic; Cecil Striker, 1019 Providence Bank Bldg., Cincinnati; Capt. W. F. Loftin (MC), U. S. Navy; Col. Charles R. Muller (MC), U. S. Army; Herbert M. Evans, Institute of Experimental Biology, University of California; Roy Hertz, National Cancer Institute.

XII. *Pathology Study Section*

Paul Cannon, University of Chicago, *Chairman*; R. D. Lillie, National Institute of Health, *Executive Secretary*; W. A. DeMonbruen, Nashville General Hospital; William H. Feldman, The Mayo Foundation; Wiley D. Forbus, Duke University; Harry Goldblatt, Cedars of Lebanon Hospital, Los Angeles; J. S. McCartney, University of Minnesota; Alan R. Mortiz, Harvard Medical School; Arnold Rich, Johns Hopkins University; James F. Rinehart, University of California; H. P. Smith, Columbia University; Col. Raymond A. Dart, U. S. Army; Cdr. R. V. Williams, U. S. Navy; C. E. DeAngelis, Veterans Administration.

XIII. *Pharmacology Study Section*

Carl F. Schmidt, University of Pennsylvania, *Chairman*; Stanford M. Rosenthal, National Institute of Health, *Executive Secretary*; H. H. Anderson, University of California Medical School; McKeen Cattell, Cornell University Medical College; E. M. K. Geiling, University of Chicago; Alfred Gilman, Columbia University; Paul D. Lamson, Vanderbilt University; Hans Molitor, Merck Institute for Therapeutic Research; M. H. Seevers, University of Michigan; Torald Sollman, Western Reserve University; H. B. van Dyke, Columbia University; Joseph A. Keeney, War Department, U. S. Army; Lt. Charles H. Hine (MC), U. S. Navy; W. Paul Briggs, Veterans Administration.

XIV. *Physiology Study Section*

Wallace O. Fenn, University of Rochester, *Chairman*; William H. Sebrell, Jr., National Institute of Health, *Executive Secretary*; Willard M. Allen, Washington University; Philip Bard, Johns Hopkins School of Medicine; Eugene F. DuBois, Cornell University; John H. Lawrence, University of California; Severo Ochoa, New York University; Carl F. Schmidt, University of Pennsylvania; Col. William S. Stone, U. S. Army; Lt. (jg) M. R. Heinrich, U. S. Navy; A. M. Walker, Veterans Administration.

XV. *Public Health Methods Study Section*

Lowell J. Reed, Johns Hopkins University, *Chairman*; Antonio Ciocco, U. S. Public Health Service, *Executive Secretary*; Gaylord W. Anderson, University of Minnesota Medical School; George Baehr, Mt. Sinai Hospital; Franz Goldmann, Yale University School of Medicine; John B. Grant, Rockefeller Foundation; Wilton L. Halverson, Department of Public Health, San Francisco; Horace Hamilton, State College Station, Raleigh, North Carolina; J. T. O'Rourke, Tufts College Dental School; Marian Randall, Visiting Nurse Service of New York; William P. Shepard, Metropolitan Life Insurance Company, San Francisco; Paul B. Magnuson, Veterans Administration.

XVI. *Radiobiology Study Section*

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XVII. *Sanitation Study Section*

V. M. Ehlers, Texas State Department of Health, Austin, *Chairman*; John Andrews, U. S. Public Health Service, *Executive Secretary*; Thomas R. Camp, Boston; C. G. Gillespie, Department of Public Health, Berkeley, California; Theodore Hatch, Industrial Hygiene Foundation; W. L. Mallman, Michigan State College; M. Allen Pond, Yale University School of Medicine; C. C. Ruchhoft, U. S. Public Health Service, Cincinnati; Maj. J. B. Baty (Ph.C), U. S. Army; Capt. Robert W. Babione, Bureau of Medicine & Surgery, U. S. Navy; Francis Carroll, Boston, Veterans Administration.

XVIII. *Surgery Study Section*

Frederick A. Coller, University of Michigan Hospital, *Chairman*; G. Halsey Hunt, National Institute of Health, *Executive Secretary*; Claude S. Beck, Western Reserve University; Oscar T. Clagett, Mayo Clinic; Robert Elman, Washington University School of Medicine; John S. Lockwood, Columbia University; Arthur Neal Owens, 1615 American Bank Bldg., New Orleans; Albert J. Scholl, 1930 Wilshire Blvd., Los Angeles; H. L. Skinner, U. S. Public Health Service, Staten Island; Barbara

Stimson, Columbia Presbyterian Medical Center, New York; Owen H. Wangensteen, University of Minnesota; Capt. W. F. James (MC), U. S. Navy; Maj. Edward H. Vogel, Jr. (MC), U. S. Army; Brian B. Blades, Veterans Administration.

XIX. *Syphilis Study Section*

J. E. Moore, Medical Arts Building, Baltimore, *Chairman*; David E. Price, National Institute of Health, *Executive Secretary*; Harry Eagle, U. S. Public Health Service; J. R. Heller, Jr., U. S. Public Health Service; John F. Mahoney, V. D. Research Laboratory, U. S. Public Health Service; Lowell J. Reed, Johns Hopkins School of Hygiene and Public Health; John H. Stokes, 4228 Spruce Street, Philadelphia; Harry C. Solomon, Boston Psychopathic Hospital; Thomas B. Turner, Johns Hopkins School of Hygiene and Public Health; Maj. L. N. Altshuler, U. S. Army; Cdr. George W. Mast, U. S. Navy; Bascom Johnson, Veterans Administration.

XX. *Tropical Diseases Study Section*

Andrew J. Warren, Rockefeller Foundation, *Chairman*; Willard H. Wright, National Institute of Health, *Executive Secretary*; Ernest Carroll Faust, Tulane University School of Medicine; William W. Frye, Vanderbilt University School of Medicine; John F. Kessel, University of Southern California; Henry E. Meleney, New York University College of Medicine; Gilbert F. Otto, Johns Hopkins University; Cornelius B. Philip, Rocky Mountain Laboratory, Hamilton, Montana; Albert B. Sabin, Children's Hospital Research Foundation, Cincinnati; Wilson G. Smillie, Cornell University Medical College; Col. Karl R. Lundeberg (MC), U. S. Army; Capt. J. J. Sapero (MC), U. S. Navy; Brig. Gen. James S. Simmons, Veterans Administration.

XXI. *Virus and Rickettsial Study Section*

John R. Paul, Yale University, *Chairman*; Norman H. Topping, National Institute of Health, *Executive Secretary*; Charles Armstrong, National Institute of Health; P. F. Clark, University of Wisconsin; John F. Enders, Harvard Medical School; Ernest Goodpasture, Vanderbilt University School of Medicine; Robert G. Green, University of Minnesota Medical School; Wm. McDowell Hammon, University of California; Geoffrey W. Rake, Squibb Institute for Medical Research; T. F. Sellers, Georgia State Department of Public Health; J. C. Snyder, Harvard School of Public Health; Max Theiler, Rockefeller Institute for Medical Research; Joseph E. Smadel, U. S. Army; Capt. James J. Sapero (MC), U. S. Navy.

Technical Papers

A Toxicity Study of Thiamine Hydrochloride

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Reingold and Webb (*5*) have recently reported that death occurred after four intravenous injections of thiamine hydrochloride (100 mg./cc.) into a human. These injections were given over a period of about one month, and it was concluded that death was due to anaphylaxis. However, the symptoms described were similar to those seen in this laboratory when a similar solution was injected intravenously into rabbits. In our work a 200- to 300-mg. total dose of thiamine usually resulted in collapse and/or death in most of the animals. If the injection was stopped before respiration ceased, the animal usually recovered within five minutes and apparently suffered no ill effects. These results were obtained over a period of eight months using 20 animals of about 3 kg. body weight. Hecht and Weese (*2*), in 1937, reported that the intravenous injection of 80 mg./kg. of thiamine hydrochloride caused no ill effects but that 160 mg./kg. caused death by paralysis of the central nervous system. Stern (*7*), in 1938, reported that death occurred in a cat given 20,000 I.U. of thiamine hydrochloride by cisternal puncture. Evidence has been presented that anaphylaxis and sensitivity both play a part in human thiamine hydrochloride toxicity (*1, 3, 4, 6, 8*).

Anaphylaxis in the rabbit is entirely different from that seen in the guinea pig or in humans. The lungs are not directly involved. The pulmonary artery is constricted, and the right auricle is engorged with blood. Respiration continues after cardiac arrest (*9*).

A group of five virgin female rabbits weighing between 1.5 and 1.9 kg. was given intravenous injections of a solution containing 100 mg./cc. of thiamine at the rate of 1 cc. every two minutes. Another group of five animals was given similar injections of a 0.35-per cent chlorobutanol solution. The solutions were given in this manner to determine which chemical was the cause of toxic manifestations seen when a solution containing 100 mg./cc. of thiamine hydrochloride and 0.35 per cent chlorobutanol (the usual commercial strength) was injected intravenously. The results of the thiamine injections are shown in Table 1. Each of the rabbits in the second group received 35 mg. of chlorobutanol (10 cc. of solution) and, when observed

over a period of one week, showed no pathological reaction to the injection.

As it had been reported that anaphylaxis plays a part in thiamine toxicity, those animals surviving were given a sensitizing dose of 100 mg. of thiamine, and one week later injected intravenously with 100 mg./cc. of thiamine solution until death occurred. The reaction of the animals was the same as previously described, but the toxic dose was almost doubled (from 375 to 500 mg./rabbit). There was no evidence of anaphylaxis, but auricular extrasystoles were seen in five of six animals injected. The usual rate was 3:1.

TABLE 1

RESULTS OF INTRAVENOUS INJECTION OF 100 MG./CC. THIAMINE HYDROCHLORIDE

Animal	Weight (kg.)	Total dose (mg.)	Results
21	1.591	220	Extreme vasodilatation at 220 mg., convulsions, cyanosis, inability to stand; animal recovered.
22	1.704	180	Vasodilatation at 120 mg., convulsions at 140 mg., death by respiratory paralysis at 180 mg. Autopsy showed lungs collapsed but normal; other organs normal; auricular extrasystoles, rate of 3:1.
23	1.818	220	Vasodilatation at 200 mg., convulsions at 220 mg., at which point respiration stopped but started again, with ensuing death by respiratory paralysis. Blood was definitely venous and the animal cyanotic. Autopsy revealed the same conditions as in #22.
24	1.591	200	Vasodilatation at 120 mg., death by respiratory paralysis at 200 mg. No convulsions; otherwise the same as #22.
25	1.704	240	Vasodilatation followed by collapse at 240 mg. No convulsions. Respiration very slow and animal cyanotic; recovered in five minutes.

Electrical stimulation of the muscles of the diaphragm showed that the muscles were still able to contract. Further, electrical stimulation of the phrenic nerve caused the diaphragm to contract, thus showing that the observed respiratory paralysis was central in origin. This could only mean that the respiratory center of the medulla was paralyzed.

CONCLUSIONS

(1) The above results are the same in every way as those observed when a solution containing 100 mg./cc. of thiamine hydrochloride and 0.35 per cent chlorobutanol was injected intravenously.

(2) The toxicity encountered upon injection of 100 mg./cc. of thiamine hydrochloride solutions is due to the thiamine content and not to the preservative.

(3) Symptoms of thiamine hydrochloride toxicity may be summarized as follows: (a) peripheral vasodilatation; (b) decreased respiration due to direct action on the respiratory center in the medulla; (c) asphyxial convulsions due to anoxia resulting from decreased oxygenation of the blood; (d) death by paralysis of the respiratory center; and (e) cardiac arrhythmias, probably due to anoxia and not a direct action of thiamine hydrochloride on the cardiac muscle or the conducting system.

(4) Anaphylaxis plays no part in thiamine hydrochloride toxicity as seen in rabbits. However, injection of a sensitizing dose apparently increases the resistance of the animal to toxic injections of thiamine hydrochloride.

(5) The lethal dose of thiamine hydrochloride by intravenous injection into rabbits is approximately 126 mg./kg.

(6) After a sensitizing dose of 100 mg. of thiamine hydrochloride the lethal dose is approximately 238 mg./kg.

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Effects of Whole-Wheat and White Bread Diets on Susceptibility of Mice to Pneumococcal Infection

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It was reported recently (*1*) that when mice are maintained on a "synthetic" diet they are much more resistant to the intraperitoneal injection of Type I, SV-1 strain pneumococcus than mice maintained on the usual laboratory diet. The explanation was advanced that the cruder diet supplies some factor (or factors) which is necessary for the rapid multiplication of the pneumococcus *in vivo*, and maintains a higher level of this factor in the tissues and fluids of the mouse than prevails during its absence from the diet. Belief in the validity of this explanation has been strengthened by the outcome of later experiments. When certain crude foodstuffs are added to the "synthetic" diets, the susceptibility of the mice to pneumococcal infection is increased. Moreover, extracts of these foods are capable of stimulating the *rate of growth* of the pneumococcus *in vitro*.[1]

[1] Unpublished experiments with Marion B. Sherwood.

Whole-wheat flour was found to be much richer than white flour in the factor stimulating pneumococcal growth *in vitro*. This suggested that mice eating whole-wheat bread might be more susceptible to pneumococcal infection than those eating white bread. The results of two experiments designed to test this possibility are shown in Table 1. The mice were maintained on either white or whole-wheat bread for 6 days before the injection of the pneumococci (10^{-4} or 10^{-6} ml. of a 17-hour culture). In both experiments the mice eating white bread were more resistant to the infection than those receiving whole-wheat bread. Thus, only 1 of 49 mice (2 per cent) on the whole-wheat diet survived the infection, whereas 20 of the 50 (40 per cent) eating white bread survived 6 days (and presumably indefinitely). In line with previous experience, the difference in response between the two dosages was small (*1*).

Obviously, these experiments provide insufficient evidence on which to decide the white vs. whole-wheat bread controversy or to base a dietary treatment of pneumonia. However, they do cast considerable doubt on one tenet of the nutritionist's credo. It is generally assumed that, when known essentials are present in equal amounts, a cruder foodstuff is to be preferred to a refined. This point of view implies that the unknown factors of the crude foodstuff are always beneficial. The assumption has an a priori validity which is supported by the history of the isolation of the vitamins and has not, up to now, been contradicted experimentally. The experiments described in this paper provide such a contradiction and cast doubt on the validity of the basic assumption. They show that, in one instance at least, the unknown factor of the crude foodstuff is more beneficial to the parasitic organism than to the animal consuming the food.

TABLE 1

EFFECT OF DIET ON THE SURVIVAL OF MICE INFECTED WITH PNEUMOCOCCUS TYPE I

Exp. No.	Diet	Dose	No. of mice	Number surviving on day indicated						Average survival (days)
				1	2	3	4	5	6	
I	Whole-wheat bread	10^{-4}	24	24	9	4	3	1	0	1.71
	White bread	10^{-4}	25	25	19	16	14	13	11	3.92
II	Whole-wheat bread	10^{-6}	25	25	9	6	2	1	1	1.76
	White bread	10^{-6}	25	25	19	12	12	10	9	3.48

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The Production of Electricity by Nerve

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Five years ago we reported (*7*) that acetylcholine produces a pronounced phase-boundary potential of negative sign at the junction of oil and saline. It was suggested that this acetylcholine potential is the basis of the electrical negativity which arises in nerve during activity. A long series of additional experiments (*1–9*) have supported this theory that the chemical mediator of the nerve impulse, acetylcholine, sets up a negative phase-boundary potential in the lipoid layer of the nerve fiber—a theory which reconciles the "chemical" and "electrical" theories of nervous transmission. In a recent review, Feldberg (*12*) states that our experiments explain the "depolarizing" action of acetylcholine at synapses and at the end-plate. The term "depolarize" does not imply that acetylcholine renders an imaginary sieve membrane permeable to ions like potassium. We have previously shown (*6, 9*) that the old Bernstein concept of an ionic sieve membrane is untenable on both theoretical and experimental grounds. Actually, the lipoid-soluble acetylcholine dissolves in the oil layer to a much greater extent than the saline, thus establishing a true phase-boundary potential which we can demonstrate on an oil layer several centimeters thick, thereby eliminating any "permeability" change in an imaginary sieve membrane.

Recently the "oil-cell" model of the nerve impulse previously described (*7*) has been modified to conform to "physiological" conditions. For example, cholesterol (from spinal cord) or brain extract is added to the oil layer, thereby increasing the phase-boundary potential. Seventeen grams of cat brain extracted with 20 cc. of guaiacol at 80° C. was cooled and filtered. The resulting brain solution in guaiacol gave 45 mv negative with 0.05 per cent acetylcholine, in contrast to 30 mv established by 0.05 per cent acetylcholine on guaiacol without brain extract. Thus, acetylcholine can produce a phase-boundary potential with brain substance.

The addition of human serum which contains "serum cholinesterase" and small amounts of "cell cholinesterase" (*14*) to the saline phase brings the "oil-cell" model still closer to living nerve. Four cc. of human serum added to 200 cc. of 0.9 per cent NaCl with bicarbonate to make the pH 8.2 (at 37° C. for 8 hours) destroys the electrogenic activity of 0.05 per cent acetylcholine as tested in the "oil-cell." This experiment shows that it is the acetylcholine and not

the esterase which produces the electrical nerve impulse. These results help to explain the absence of severe symptoms in persons whose esterase is reduced to only 1 per cent of its normal value (*10*). In fact, Fraser (see *12*) nearly 80 years ago showed that eserine does not depress nerve-trunk activity. It is possible, however, that under certain conditions eserine may block impulse transmission by the negative phase-boundary potential established in contact with lipoids (*5*).

The descending part of the electrical wave in the electric fish and in the ganglion (*12*) is prolonged by eserine because the acetylcholine phase-boundary potential persists for a longer time, but no experiments have shown modification of the descending phase of the spike potential in nerve by eserine or other anticholinesterase drugs.

The rise and fall of the spike potential in peripheral nerve can be duplicated in the oil-cell by placing the acetylcholine first on one side and then on the opposite side of the oil layer. With resin in the oil a film less than 0.1 mm. thick can be formed by pressure on the saline on one side. Under these conditions a potential of 30 mv, produced by 0.05 per cent acetylcholine, fell to zero in 4 hours, due to the penetration of the alkaloid to the opposite side. With very thin films of oil the spike rose and fell too fast for measurement with the potentiometer attached to the "oil-cell."

Careful measurements of the phase-boundary potential of possible products of nerve metabolism (potassium, lactic acid, lactate, phosphate, acetate, choline, citric acid) have shown that acetylcholine has a much greater electrogenic property and is the only substance so far studied capable of producing the action current in nerve. For example, as much as 1 per cent KCl is necessary to produce 10-mv negativity on cholesterol in guaiacol, and 5 per cent lactic acid produces only 10-mv positivity in contrast to the pronounced effect of dilution of acetylcholine previously described (*7*). There remains the possibility that the small negative after-potential is set up by choline and the two small positive after-potentials by acetate and phosphate.

The distinction between cholinergic and adrenergic nerves receives its first explanation by the phase-boundary theory. Triglyceride oils (*2, 4*) establish potential with sympathomimetric but not with parasympathomimetric drugs. We have recently found that choline as well as acetylcholine is inactive on triacetin (which gives potentials with epinephrine, benzedrine, etc.). When present, the phase-boundary potentials of epinephrine and acetylcholine are both negative, which suggests that these substances may potentiate under certain conditions, which is indeed the case (*11*).

The study of phase-boundary potential can be applied directly to nerve. Frog sciatic nerve is immersed in isotonic glucose for 1–2 hours (to eliminate short circuits by salts). The ends are tied, and the nerve forms a loop between two watch glasses of isotonic glucose connected to our potentiometer as previously described for the oil-cell (*7*). Addition of 1:160,000 acetylcholine to the solution bathing the part of the nerve in one dish sets up a phase-boundary potential of 10-mv negativity (which decreases in magnitude with time). Lorente de Nó (*13*) did not detect electrical changes in nerve treated with acetylcholine, since he failed to use isotonic sugar as recommended by Netter (*15*).

The experiments reported above support the theory that the electrical nerve impulse is a phase-boundary potential produced by acetylcholine in contact with nerve lipoid.

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Scanning Science—

The American Physiological Society is holding its ninth annual meeting at Boston and Cambridge on December 29th and 30th. Headquarters will be at the Hotel Brunswick. Those who require apparatus or other necessities for making demonstrations may communicate with Dr. H. P. Bowditch. R. H. Chittenden is president of the Society and Frederic S. Lee is secretary.

The American Psychological Association will meet at the same time and Prof. G. S. Fullerton, its president, will make an address on the 29th.

The American Society of Naturalists, also meeting at the same time, will join with the Psychologists in a discussion of "Inheritance of Acquired Characteristics" in which J. M. Macfarlane, C. S. Minot, E. D. Cope and William James will take part. Prof. E. B. Wilson will lecture on "Recent Developments of the Cell Theory."

—11 December 1896

News and Notes

Boston Meeting, Corrections and Additions

General Sessions—The principal general session, at which the address of the retiring president, Charles F. Kettering, will be delivered, is to be held on Friday evening, 27 December, instead of on 26 December, as previously announced.

At the General Technical Session, Friday morning and afternoon, 27 December, Rear Admiral William S. Parsons, Director of Atomic Defense, U. S. Navy, will replace Vice-Admiral W. H. P. Blandy, previously scheduled to speak.

The National Association of Science Writers—The symposium on "The Quality of Science Writing Now Being Presented to the American Public," in which members of the Association have been invited to participate, is to be held at 8:00 P.M. on 28 December, 46 Dunster Street, Cambridge.

Sigma Delta Epsilon—The luncheon for all women in science will be in the Monaco Room of the Lenox Hotel on Sunday, 29 December.

Press Room—The Press Room for the Boston meeting will be in Parlor F of the Hotel Statler. The Association's representative in charge of press relations will be Sidney S. Negus, professor of chemistry, Medical College of Virginia, Richmond.

About People

All of the American Nobel Prize winners received their awards in Stockholm on 10 December. H. J. Muller, P. W. Bridgman, and J. B. Sumner left New York by plane on 5 December; Wendell M. Stanley and John Howard Northrop had left earlier. All of them will remain in Sweden for some time and will address the sections of the Nobel Committee on Physiology and Medicine, Physics, and Chemistry, on dates not yet announced.

A $1,000 prize will be presented to James Graham Chesnutt, winner of the 1946 AAAS-George Westinghouse Science Writing Award, at a luncheon at the Hotel Statler, Boston, on 27 December. Mr. Chesnutt received the prize for a story entitled, "Bubonic Plague Preventive Proven in Animal Tests Here," dated 6 September 1946, published in the *San Francisco Call-Bulletin*. The article describes work conducted by Karl F. Meyer, director of the Hooper Foundation for Medical Research of the University of California, in developing a vaccine to be used against the bacillus which causes bubonic, septicemic, and pneumonic plagues, all commonly known as "Black Death."

The judges recommended that two other writers be given honorable mention: Herbert A. Shaw, Jr., of the *Dayton Daily News,* for his story, "Pollinosis Isn't Something 'To Be Sneezed At'!"; and Stephen White, of the *New York Herald Tribune,* for his story, "Radar Contact With the Moon Is Made at Army Laboratory."

The selection of the winning entry was made on 4 December by a committee appointed by AAAS and headed by Morris Meister, president of the National Association of Science Teachers. The other judges were: Wilbur Forrest of the *New York Herald Tribune*; W. S. Gilmore of the *Detroit News*; Sally Butler, president of the National Federation of Business and Professional Women's Clubs, Inc.; Elbert D. Thomas, senator from Utah; A. J. Carlson, past president of AAAS; and James B. Conant, president of Harvard and president of AAAS for 1946.

In this first year of the contest there were 137 entries. Dr. Meister said that the following criteria were used in the judging process: (1) Does the story meet the usual standards of newspaper writing?; (2) does the writer show originality and initiative in getting the story and in his method of presenting it?; (3) does it meet the standards of scientific accuracy expected for the general reader?; (4) does it show the viewpoint of science, dramatizing the process by which scientific achievements are made, as well as the end products of that process?; and (5) does the reader gain facts, information, and better understanding about important ideas in science?

One feature of the contest, which will be conducted again next year, was that the judges had only the masked stories before them; they were not aware, until after the final selections had been made, who wrote the stories or in what newspapers they were published.

Charles J. Willard is now acting chairman of the Department of Agronomy at The Ohio State University, succeeding R. Donald Lewis, who resigned last summer to become director of the Texas Agricultural Experiment Station. Dr. Willard has been associated with Ohio State since 1917 and has also served for some years with the Ohio Agricultural Experiment Station.

William H. Adolph, during the war acting professor of nutrition and biochemistry at Cornell University,

is returning to his prewar post as professor of biochemistry and chairman of the Department of Chemistry at Yenching University, Peiping, and expects to leave for the Far East this month. Dr. Adolph was interned by the Japanese during the early months of the war and was repatriated to this country on the *Gripsholm*.

Cyrus O. Guss, of the Forest Products Laboratory, Madison, Wisconsin, has been appointed assistant professor of chemistry at the University of Southern California.

G. R. Mandels, formerly of the Department of Botany, Cornell University, has been made assistant mycologist at the Biological Laboratories, Quartermaster Depot, Philadelphia.

Announcements

The American Institute of Nutrition is requesting nominations for the Borden Award in Nutrition, given in recognition of distinctive research by investigators in the United States and Canada which has emphasized the nutritive significance of the components of milk or of dairy products. The award will be made primarily for the publication of specific papers, but the judges may recommend that it be given for important contributions over an extended period of time. The award may be divided between two or more investigators. Employees of the Borden Company are not eligible for the honor. The formal presentation will be made at the annual meeting of the Institute in Chicago, 18–22 May 1947. To be considered for the award, nominations must be in the hands of the chairman of the Nominating Committee by 15 January. The nominations, accompanied by such data relative to the nominee and his research as will facilitate consideration for the award, should be sent to: Genevieve Stearns, Chairman, Nominating Committee, College of Medicine, State University of Iowa, Iowa City, Iowa.

Pacific Science, an illustrated quarterly devoted to the biological and physical sciences of the Pacific area, will be published by the University of Hawaii beginning in January 1947. This magazine offers an opportunity for scientists to publish research papers and notes dealing with the Pacific region. The editorial board, consisting of specialists from the University of Hawaii and other Island institutions, includes: A. Grove Day, editor-in-chief; E. H. Bramhall, Vernon E. Brock, Harry F. Clements, Robert B. Dean, Charles H. Edmondson, Harvey I. Fisher, F. G. Holdaway, M. B. Linford, A. J. Mangelsdorf, Harold St. John, and Chester K. Wentworth.

The first issue of *Pacific Science* will contain an illustrated paper on the "tidal wave," or tsunami, of 1 April 1946, by G. A. MacDonald, F. P. Shepard, and D. C. Cox, and a study by Harold St. John pointing out the fact that, contrary to local opinion, sandalwood is still abundant on the Waianae and Koolau mountains of Oahu. Other material of local interest includes notes on the red-billed Leiothrix (hill robin) in Hawaii, and an article on dolomitization in semiarid Hawaiian soils. *Pacific Science* will be issued in January, April, July, and October of each year. Contributions should be addressed to A. Grove Day at the University, and subscriptions ($3.00 a year) may be placed through the University's Office of Publications.

The chemistry and physics of high polymers is the topic of a series of lectures being given at the National Bureau of Standards, according to an announcement by E. U. Condon, director. The lectures, arranged by Robert Simha, of the Division of Organic and Fibrous Materials, are being held from 7:00–9:00 P.M. in Room 214 of the Chemistry Building, National Bureau of Standards, and are open to the public without charge. The first lecture was held on 22 November, and the remainder of the program is as follows: 13 December, "Visco-Elastic Properties of Polymer Solutions," J. D. Ferry, University of Wisconsin; 22 January, "On Quantum Mechanisms of a Macroscopic Scale," F. W. London, Duke University; 30 January, "Applications of Magnetochemistry to Polymers and Polymerization," P. W. Selwood, Northwestern University; 27 February, "Physical Chemistry of Collagen," J. H. Highberger, General Dyestuff Corporation; 6 March, "Solution Properties of Cellulose Derivatives—Correlation With Physical Properties," H. M. Spurlin, Hercules Powder Company; 28 March, "Effects of Low Temperature on High Elasticity of Rubbers," S. D. Gehman, The Goodyear Tire and Rubber Company; 24 April, "Elasticity and Plasticity of High Polymers," H. Leaderman, The Firestone Tire and Rubber Company; 8 May, "Electrical Properties of Polymers," R. M. Fuoss, Yale University; 29 May, "Polar Coordination in Solid Polymers," W. O. Baker, Bell Telephone Laboratories; 5 June, "Optical Investigations on Polymers," W. Heller, Wayne University; and 12 June, "Discoloration of Polymers," R. F. Boyer, The Dow Chemical Company.

The 38th annual field trip of the New England Geologists' Conference, the first since 1940, was held in the Mount Washington area of the White Mountains on 5–6 October and was attended by more than 125 geologists, representing 24 colleges and universities. Marland P. Billings, Harvard University, and Katharine Fowler-Billings and Randolph W. Chapman, The Johns Hopkins University, were the leaders of the trips. Three trips were conducted on Saturday,

5 October. Two of the groups ascended Mt. Washington, while the other group visited points of geological interest in the Percy, New Hampshire, quadrangle. On Saturday evening, the assembled geologists held an informal meeting at the Glen House. The meeting was under the charge of Lloyd W. Fisher, executive officer of the Conference. Guy Shorey, commercial photographer, Gorham, New Hampshire, entertained the group with natural color slides of the area in which the trips were taken. Discussions on the field trips were conducted by the three leaders. It was voted by the group to hold their 1947 field excursion in the Boston area under the direction of Robert L. Nichols, of Tufts College.

The fifth botanical expedition of Chicago Natural History Museum to Central America got under way recently when Paul C. Standley, curator of the herbarium, went to New Orleans to embark on the steamship *Junior* of the United Fruit Company. Dr. Standley will remain in the field through the greater part of 1947. He will make comprehensive collections of the flora from the Pacific Slope in Honduras, El Salvador, and Nicaragua. Four previous expeditions by Dr. Standley and Julian A. Steyermark, assistant curator, explored the 22 departments of Guatemala in prewar years.

The Medical College of Alabama announces the receipt of two grants made to J. K. Cline, associate professor of biochemistry. Distillation Products, Inc., awarded him $2,500 for research in Vitamin E therapy, and a grant of $7,500 by the Research Corporation for a study of antianemic substance was made last month. Dr. Cline, formerly director of the laboratory of the Nutrition Clinic at the Hillman Hospital, was appointed to the faculty of the Medical College in March 1946.

Additions to the faculty at the Utah State Agricultural College are Delbert A. Greenwood, professor of chemistry, formerly research associate in pharmacology at the University of Chicago; Clyde Biddulph, assistant professor of physiology, formerly postdoctorate fellow at the University of Wisconsin; and Winslow W. Smith, professor and head of the Department of Bacteriology and Public Health, formerly professor of bacteriology, University of Southern California.

The University of Tennessee College of Medicine, Memphis, announces the following appointments: Victor C. Myers, Western Reserve University, visiting professor of chemistry; Joseph A. Brady, fellow in neurosurgery, Mayo Clinic, visiting instructor in anatomy; John L. Wood, formerly of Cornell University Medical School, associate professor of chemistry; J. B. Walker, instructor in chemistry; Edwin D. Murphy, formerly of Yale University, instructor in pathology; R. R. Overman, assistant professor of physiology; Rulin Bruesch, professor of anatomy; R. H. Alden, associate professor of anatomy; W. L. Whittemore, recently discharged from the Navy, and J. H. Bushart, released from the Army, instructors in anatomy.

The University of Miami Marine Laboratory at Coral Gables, Florida, has announced the appointment of the following to membership on an advisory committee: Paul S. Galtsoff, U. S. Fish and Wildlife Service; Daniel Merriman, Bingham Oceanographic Laboratory; Albert Eide Parr, American Museum of Natural History; and Waldo Schmitt, Smithsonian Institution. The committee will work in collaboration with the director, F. G. Walton Smith, to promote the development of tropical marine biology and oceanography and to ensure cooperation and integration of the research program with that of other institutions.

A Conference on "The Mechanics of Development" will be held by the New York Academy of Sciences at the American Museum of Natural History on 10–11 January 1947 under the chairmanship of Roberts Rugh, New York University. The program follows: 10 January, 9:30 A.M.—"The Egg in Maturation, Fertilization, and Early Cleavage," L. G. Barth, Columbia University, presiding, with papers by Donald P. Costello, University of North Carolina, G. Fankhauser, Princeton University, and J. Holtfreter, University of Rochester; 1:30 P.M.—"Gastrulation, Determination, and Localization," E. G. Conklin, Princeton University, presiding, with papers by D. Rudnick, E. J. Boell, and J. S. Nicholas, Yale University; 11 January, 9:30 A.M.—"Regeneration," Ross G. Harrison, Yale University, presiding, with papers by S. M. Rose, Smith College, S. R. Detwiler, Columbia University, and L. S. Stone, Yale University. Embryologists who are interested in attending this symposium may arrange for admission tickets by sending their requests to: Mrs. Eunice Miner, New York Academy of Science, American Museum of Natural History, New York City.

Elections

At the seventh annual meeting of the Sigma Xi Club of Hawaii, on 28 October, the following officers were installed: president, W. H. Eller; vice-president, M. B. Linford; and secretary-treasurer, R. W. Hiatt. The retiring president, C. E. Pemberton, presented the address of the evening, entitled "A Study in Insect Ecology Within the Nests of the Mud-Dauber, *Sceliphrons cementarium.*"

Frederick R. Lack, vice-president and a director of the Western Electric Company in charge of its Radio Division, was elected president of the American Standards Association at its 28th annual meeting, held at the Waldorf-Astoria Hotel on 21–22 November.

The Carolina Geological Society, at its seventh annual meeting held at Shelby, North Carolina, on 16 November, elected the following officers: president, J. L. Stuckey, State College, Raleigh, North Carolina; and vice-president, W. B. Cormack, University of South Carolina, Columbia.

Recent Deaths

Robert Edward Lyons, 77, died on 25 November in Bloomington, Indiana. Dr. Lyons, who became professor emeritus in 1938, took over the Chemistry Department of the University of Indiana at the age of 25 and headed it for 43 years.

David Hunt Linder, 47, member of the Department of Biology, Harvard University, since 1931, died at the Baker Memorial Hospital, Boston, on 10 November following a heart attack. Dr. Linder was also curator of the Farlow Herbarium and Library and during the war aided the Quartermaster Corps in its investigations of tropical molds.

Nellie E. Goldthwaite, 83, head of the Chemistry Department of Mount Holyoke College from 1897–1905, died on 25 November in South Hadley, Massachusetts. After leaving Mt. Holyoke, Dr. Goldthwaite taught at the Universities of Illinois and New Hampshire and at the Colorado College of Agriculture, from which she retired in 1925.

Otway H. Brown, 69, died on 31 October at Cape May, New Jersey. At the time of his death he was curator of the Cape May Geographic Society and had recently completed his private herbarium of 5,000 specimens of Cape May County.

Lawrence V. Redman, 66, plastics chemist, died in Toronto on 25 November. In 1931 he was elected president of the American Chemical Society, serving in the Chicago section and later in the New Jersey section.

Lorene Teegarden, 50, psychologist for the Vocational Rehabilitation Service, Washington, D. C., died on 2 November.

Charles F. Hindle, 71, inventor of an electrocardiograph which has been used for the last 30 years for the recording of heart beats, died on 23 November in River Forest, Illinois. A portable cardiograph, which he designed in 1932, is now made by the Beck-Lee Corporation of Chicago, of which his son, Frederick, is superintendent.

The Ninth Washington Conference on Theoretical Physics

"The Physics of Living Matter" was the subject of discussion by a group of investigators in biology and theoretical physics in a series of informal meetings at the Ninth Washington Conference on Theoretical Physics, held on 31 October and 1–2 November in Washington, D. C., under the joint auspices of George Washington University and the Carnegie Institution of Washington.

Previous to the Eighth Conference on Theoretical Physics, held in April 1942, these meetings were annual events and were devoted to such subjects as "The Theory of Fundamental Particles," "Astrophysics," and "The Interior of the Earth."

The subject of the current Conference was chosen in response to widespread interest among theoretical physicists in biological problems. The main objective of the meeting was to bring together leaders in biology and physics, giving them ample opportunity to know each other and to exchange ideas, with a view to the possibility of closer collaboration in the future.

Among the fields touched upon were the action and reduplication of genes and chromosomes, the tobacco mosaic virus, the mutant strains of coli bacteriophage, the energy-rich phosphate bonds, the extranuclear hereditary factors as links in the genetic control of enzymatic action, and the problem of photosynthesis.

The biologists participating in the meetings generously contributed by presenting at length a number of fundamental biological facts. The physicists expressed their interest in the situations outlined to them by asking specific questions, and making comments and tentative suggestions. At the conclusion of the Conference many of the physicists indicated their interest in considering further the "Physics of Living Matter," while others chose particular topics which they intend to study.

Representatives from 24 universities, research organizations, and governmental bureaus took part in the Conference. Among those attending from outside Washington were: G. W. Beadle, Jesse W. Beams, Niels Bohr, C. F. Cori, Max Delbruck, M. Demerec, John T. Edsall, James Franck, S. Karrer, Walter J. Kauzmann, John G. Kirkwood, F. W. London, H. J. Muller, E. O. Salant, F. O. Schmitt, S. Spiegelmann, W. M. Stanley, Leo Szilard, Edward Teller, John von Neumann, and H. Weyl.—*G. Gamow* and *P. H. Abelson.*

In the Laboratory

A Microanalyzer for Very Small Gas Samples (0.4-1 mm.^{3})

W. E. Berg

Department of Biology, Stanford University

The apparatus to be described was developed to determine the composition of small bubbles formed in animals decompressed to simulated high altitudes (*1*). It is, however, suitable for more general use in biological research or in any situation requiring analysis for CO_2 and O_2 in very small samples of gas (0.4–1 mm.^{3}). Modification of the procedure might adapt it to other gases as well. The constant-pressure, capillary-tube method is used, following Krogh (*3*), Scholander (*4*), and others (see review by Hartridge, *2*), but modifications in construction and technique permit more rapid analyses of smaller volumes of gas. The apparatus has the advantages of simple construction and rapid operation.

Construction

The analyzer (Fig. 1) consists of a 6-inch length of capillary thermometer tubing (0.11-mm. bore) with an open, bell-shaped absorption chamber blown at one end. A short piece of rubber pressure tubing, plugged with a short glass rod, fits over the other end and is provided with a screw clamp. The capillary tubing is surrounded by a water jacket to minimize temperature fluctuations.

Operation

To prepare for an analysis, the rubber tube is fitted over the end of the capillary of the analyzer and is filled with a saturated aqueous solution of LiCl.[1] The glass rod is then pushed into the open end of the rubber tube and LiCl solution is forced through the capillary to fill the absorption chamber, in which it is retained by surface tension. The analyzer is held vertically with the absorption chamber downward, and the bubble of gas to be analyzed is introduced into the chamber from a small pipette containing LiCl solution. If extraneous fluids (such as blood) must be removed from the bubble, it is first washed in a small dish of LiCl solution, from which it is transferred into the absorption chamber. The analyzer is held vertically, and the bubble rises to the constriction of the tube at the top of the absorption chamber and is slowly and carefully drawn into the capillary by opening the screw clamp. It is necessary to standardize the rate at which the bubble is drawn into the capillary in order to avoid variations in the amount of liquid retained on the capillary wall. With practice, the gas sample can be transferred into the analyzer in a few seconds.

The length of the column of gas, which is proportional to its volume, is then measured on the graduated scale of the thermometer tubing. It varies about 1 per cent, depending on whether it is moved toward or away from the absorption chamber. By averaging several readings the error of this measurement is reduced to 0.1–0.2 per cent.

Having measured the length of the entire gas sample, the next step is to remove the CO_2 and measure the length of the remainder. This is accomplished by substituting a solution of LiCl + KOH for the LiCl solution in the absorption chamber and forcing the sample of gas out into this new solution. The KOH absorbs the CO_2 while the LiCl impedes the exchange of other gases by diffusion. Absorption of the CO_2 is completed in a few seconds. The bubble is again drawn into the capillary and measured. If the O_2 content of the sample is to be determined, alkaline pyrogallol solution (which absorbs O_2) is substituted in the absorption chamber, and the procedure for absorption is repeated with rotation of the analyzer for 20 seconds, in this case, to facilitate absorption. The operation should be repeated a second time to be sure that the absorption of O_2 is complete. The percentages

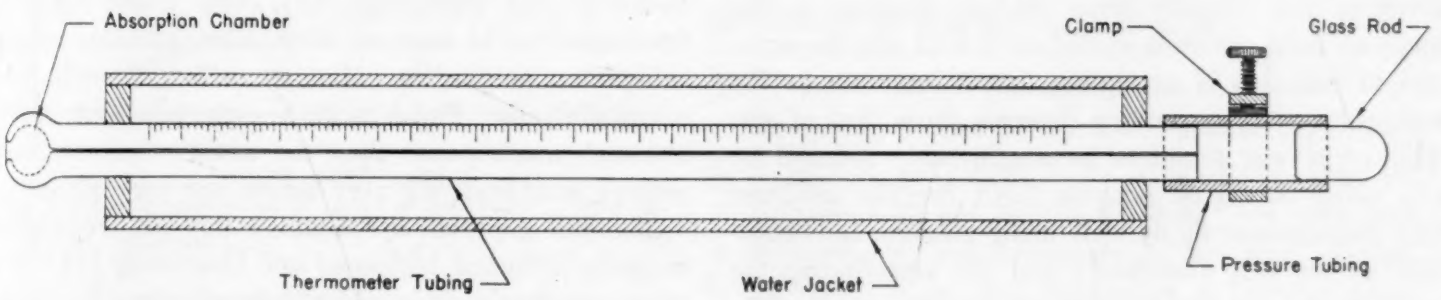

Fig. 1

[1] Gases are relatively insoluble in saturated LiCl solution, which therefore reduces errors due to loss by diffusion.

of CO_2 and O_2 in the original sample are calculated from the changes in length of the gas column, and the volume of the bubble is calculated from the length of the gas column (40–100 mm.) and the cross-section area of the capillary (.0095 mm.^{2}). A complete analysis can be performed in 10–15 minutes.

After each analysis the apparatus is cleaned by drawing tap water and then cleaning solution through the capillary, rinsing with tap and distilled water.

Accuracy

The accuracy of analysis depends primarily on the amounts and kinds of gases in the sample. Other important factors, subject to a considerable degree of control, are (1) alteration of the sample through gaseous exchange with the analyzer fluid by diffusion; (2) changes in the water vapor tension in the bubble when in contact with solution of different osmotic pressure; (3) rate at which the bubble is drawn into the capillary; and (4) reading error. In actual practice, diffusion of gases is found to be the greatest source of error. If the composition of the bubble diverges only slightly from the gas tensions in the analyzer fluid, which is equilibrated with air, the error due to diffusion is negligible, but it increases as the composition of the sample diverges from that of air. This error was found to be considerably reduced by (1) using saturated aqueous LiCl for the analyzer and transference fluids; (2) using alkaline LiCl solution as the CO_2 absorbent; and (3) introducing the gas sample into the analyzer as rapidly as possible.

TABLE 1

Sample No.	Vol. of bubble	Known composition of gas mixture*			Composition as measured in analyzer		
		CO_2	O_2	N_2	CO_2	O_2	N_2 (by difference)
	(mm.^{3})	(%)	(%)	(%)	(%)	(%)	(%)
1	1.43				...	20.7	79.3
2	0.42	0.03	20.95	79.02	...	21.0	79.0
3	1.41				...	20.9	79.1
4	0.78		(air)		...	21.1	78.9
1	0.55				5.0	91.1	3.9
2	0.45	5.29	93.63	1.08	4.9	89.6	5.5
3	1.03				5.4	92.6	2.0
4	0.40				5.4	92.1	2.5
1	0.50				14.5	8.1	77.4
2	0.57	14.90	7.65	77.45	14.7	8.0	77.3
3	0.45				14.4	7.9	77.7

* Determined by means of the Haldane gas analysis apparatus.

Greater accuracy could be obtained by equilibrating the solutions with a gas mixture of composition approximating that of the sample to be analyzed. Under most favorable conditions the error of analysis is less than 0.3 per cent. Under less favorable conditions it increases but is not unreasonable considering the extremely small volumes of gases analyzed.

Typical analyses of air and known gas mixtures by this method are given in Table 1.

References

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3. Krogh, A. *Skand. Arch. Physiol.*, 1908, **20**, 279.
4. Scholander, P. F. *Rev. sci. Instr.*, 1942, **13**, 264.

A New Method for the Purification of Arginase

C. Bertrand Thompson[1]

Division of Biochemistry, University of California Medical School, Berkeley

Many and varied studies on arginase can be and have been made on very crude solutions. With two exceptions, most preparations reported from 1924 (*3*) to 1944 (*2*) were essentially extractions in glycerol, with reduction in large volume of acetone. The exceptions were Edlbacher and Simons (*1*), who tried adsorption on alumina C and Willstätter kaolin, and Richards and Hellerman (*5*), who made repeated fractionations in acetone, ammonium sulfate, sodium salicylate, and sodium alizarin sulfonate, with frequent dialyses. These methods gave products which, although much purer than the usual solutions, were neither comparatively very active nor very pure.

The first reported systematic study of preparative methods is that of Mohamed and Greenberg (*4*). The procedure finally adopted by them consisted in extractions and fractional precipitations in sodium acetate, lead acetate, ammonium sulfate, adjustment to pH 8,

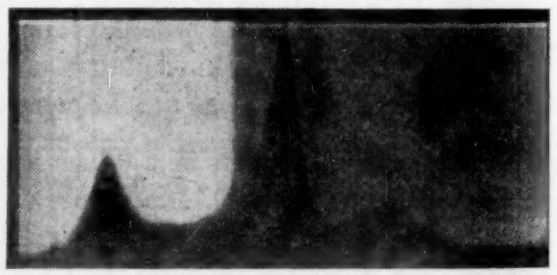

Fig. 1. Tiselius curve of purified arginase in pH 6.2 phosphate buffer μ0.10; 205 minutes at 5.8 volts/cm.; $U_F = 6.3 \times 10^{-5}$; $U_S = 2.3 \times 10^{-5}$. (Courtesy of Dr. C. H. Li, Institute of Biological Research, University of California.)

reduction in acetone, and solution in pH 7 phosphate buffer. The final product, a green-brown solution, showed by electrophoresis in the Tiselius apparatus the presence of three or four constituents. Catalase was a definite contaminant of the mixture. The problem remaining, therefore, was that of freeing the preparation of catalase and other proteins. It was

[1] The author wishes to thank the Division of Biochemistry, University of California Medical School, for the use of its laboratories and facilities, and Prof. D. M. Greenberg, Division of Biochemistry, for helpful suggestions and advice.

at this point that the present investigation was undertaken by the author.

The addition of manganese or cobalt salts, brought to pH 4, with the immediate addition of an excess of phosphate buffer of pH 9 cleared the solution, apparently by coprecipitation, of all colored substances, with loss of only 35–45 per cent of activity. Details of the method will be given elsewhere.

The Tiselius curve (Fig. 1) shows the presence of only two constituents, presumably only one besides the arginase. The arginase is found in the slow fraction.

The spectrophotometric curve (Fig. 2) of the cobalt-purified solution (A) and a solution before purification (B) shows a considerable drop in the peak at 412 mμ.

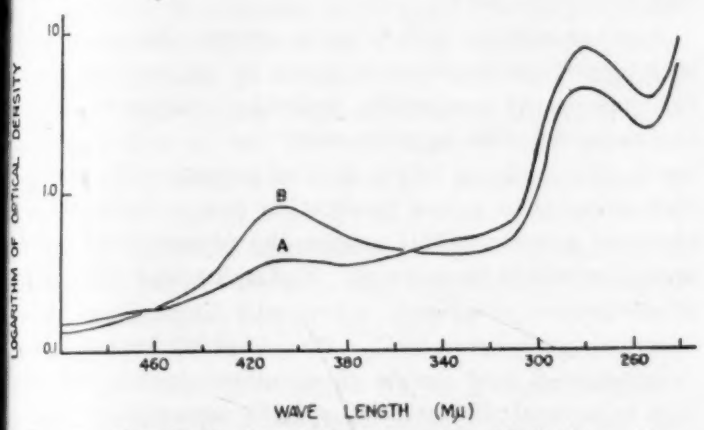

FIG. 2. Spectrophotometric curve of purified (A) and unpurified (B) arginase. (Courtesy of L. A. Strait, University of California Hospital.)

It may be considered established that arginase is a colorless enzyme, with the properties of an albumin. Further studies are under way to complete the purification and to increase the yield.

TABLE 1

EFFECT OF DIVALENT CATIONS

Salt	Clarification	Yield
Co^{++}	Excellent	Good
Mn^{++}	Good	"
Ni^{++}	"	"
Cd^{++}	"	Poor
Zn^{++}	"	"
Sr^{++}	Slight	Good
Ba^{++}	"	Fair
Ca^{++}	"	"
Mg^{++}	"	"
Pb^{++}	"	Poor

Another series of tests shows similar effects in varying degrees from the following divalent cations: barium, cadmium, calcium, lead, magnesium, nickel, strontium, and zinc. Cobalt, manganese, and nickel give the best combination of clarification and yield; cadmium and zinc give excellent clarification but less than half the yield; while barium, lead, magnesium, and strontium give comparatively slight clarification and widely varying yields (Table 1).

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Letters to the Editor

On Filing Reprints

L. R. Richardson (*Science*, 1946, **104**, 181–182) explained a method of filing which he has found to be very satisfactory for a reprint collection. He recommended filing by author in large, 10- by 13-inch, open-ended manila envelopes, one author per envelope. There seem to be some objections to this system. These will be mentioned and another system proposed.

In the first place, many bookcases are not provided with sufficient clearance between shelves so that the 13-inch envelopes can be placed on end as suggested, and if they are, a lot of potential shelf space is lost. Secondly, a great percentage of reprints do not require envelopes of such size, but because of the occasional one of large format or the possible future one, extra room must be provided in all envelopes. Thirdly, many reprint collections contain only one or two papers by some authors and dozens by others. A manila envelope for a single paper might be considered extravagant both in money and space, while a prolific writer would require many envelopes. The last objection is that the reprints stand in a vertical position, which is not the best from the point of view of preservation, particularly for old papers.

After having tried several systems, the present writer has found one that is workable and conserving of space. The fundamental assumption is that the place of original publication rather than subject or author is the best basis for filing. This method does away with the difficulty of subject classification and with the problem of joint authorship—the best-known author's name does not always come first. Under this system papers are filed with others of the same size, since journals do not constantly change their format, and it is not necessary to provide unnecessary space for the occasional large paper as under the system proposed by Richardson.

Cardboard boxes with deep covers are used, to which are pasted labels listing the periodicals contained. Within the box, papers are filed by date of publication. Reprints

from some journals may be so abundant that more than one box is needed; on the other hand, some boxes may contain the reprints from three or more journals. An unclassified box takes care of the occasional reprint from journals represented by only a few papers which can easily be moved to a classified box as soon as their number justifies. Large boxes are provided for those publications using a big format and small for those of small format. Under this system the reprints lie flat, are well protected, and widely spaced shelves are not needed.

As in Richardson's system, a card catalogue or bibliography is needed, but once the reference has been found, it is as easy to go to the correct box by publication as it is to go to the envelope by author.

LAWRENCE WHITCOMB
Department of Geology, Lehigh University

New Data on the Extraction of B_1 From Natural Material (Yeast)

Investigation was made to determine the most suitable conditions for the extraction of B_1 from yeast.

In a series of assays, using yeast from the same container and using the same enzyme (papain) but a different pH with each assay, it was found that optimum results were obtained at pH 1.0–1.5.

At the same time it was confirmed that synthetic B_1 is best conserved at pH 4.0–4.5.

For the checking of the B_1 the colorimetric method of Melnick and Field was used.

Further work is needed to determine whether the findings apply to the extraction of B_1 from other natural materials; also, on the use of different enzymes or a combination of enzymes.

J. OSMAN

S. O. Barnes & Son
Gardena, California

The Rh System in the Chimpanzee

The present writer's theory of multiple allelic genes, to account for the hereditary transmission of the Rh-Hr blood types, has received adequate confirmation from family and statistical studies (A. S. Wiener, E. B. Sonn, and H. R. Polivka. *Proc. Soc. exp. Biol. Med.*, 1946, **61**, 382). On the other hand, no substantial evidence has been adduced to support Fisher's theory of gene triplets, which only leads to contradictions and paradoxes (A. S. Wiener. *Brit. med. J.*, 1946, **1**, 982; J. Murray. *Brit. J. exp. Path.*, 1946, **27**, 102). A new argument for Fisher's theory has now been advanced in your columns by Mourant and Race (*Science*, 1946, **104**, 277).

M. Wade and I (*Science*, 1945, **102**, 177) reported that the bloods of every one of 15 chimpanzees tested did not absorb anti-Rh′, anti-Rh″, or anti-Rh_o agglutinins from human antisera, but did absorb anti-Hr′. This is confirmed by tests on a single additional chimpanzee by Mourant and Race, who also report that the blood of their chimpanzee did not absorb the anti-Hr″ agglutinin. Based on this finding, Mourant and Race conclude that the factors Rh″ and Hr″ are absent from chimpanzee blood and suggest that the hypothetical locus E-e of Fisher is lacking in this species. They consider this apparent separation of one gene pair from Fisher's three sets of hypothetical genes an argument favoring Fisher's theory of closely linked genes, as against my multiple allele theory.

The reasoning used by Mourant and Race has a number of fallacies which can best be demonstrated by citing analogous observations involving other blood agglutinogens. Rhesus red cells are not clumped by, nor do they absorb, human anti-Rh_o agglutinins, which, according to Mourant and Race, would indicate that the Rh_o factor is entirely lacking in this species. However, the original antisera for detecting the Rh_o factor were prepared by injecting Rhesus blood into rabbits and guinea pigs; in fact, that is how the Rh factor got its name. The correct conclusion is that Rhesus blood does not contain a factor identical with human Rh_o—only a related factor, that is, an Rh_o-like factor. Similarly, it seems highly likely that chimpanzee blood actually does contain Rh″-like or Hr″-like factors, or both.

Another obvious fallacy is to assume that every separate agglutination reaction given by an antigen proves the presence of comparable separable components within the antigen. The agglutination test is merely a diagnostic test, and one might just as unreasonably conclude that every time a new qualitative test is devised for a chemical substance this proves the presence of another structure within its molecule. K. Landsteiner (*Specificity of serological reactions.* (Rev. ed.) Cambridge, Mass.: Harvard Univ. Press, 1945. Pp. 114–116) has repeatedly demonstrated how simple chemical compounds can give rise to several distinct but specific immune antibodies, and he has also demonstrated that the number of qualitatively different antibodies is not necessarily correlated with the existence of distinct structures within the antigen molecule. If we were to apply Mourant and Race's arguments in the case of the A-B-O blood groups and the M-N types, we would be faced with a number of queer paradoxes. Studies on the evolution of the M agglutinogen reveal the existence of at least four distinct partial antigens in the human M agglutinogen and two partial antigens in the N agglutinogen (A. S. Wiener. *Amer. Nat.*, 1943, **77**, 199). According to Fisher, it would therefore be necessary to postulate that agglutinogen M of human blood is determined by a gene complex, $M_iM_{ii}M_{iii}M_{iv}$, while agglutinogen N is determined by a linked gene complex, N_iN_{ii}. This leads to a situation where corresponding portions of a pair of homologous chromosomes are not homologous, and, if this conclusion were correct, it would be very strange that in millions of tests no evidence of crossing-over, such as a blood $M_iM_{ii}N_{ii}$, has ever been obtained. It seems much more reasonable to conclude that the complicated M and N agglutinogens of human blood are each determined by corresponding genes forming an allelic pair, in accordance with the generally accepted theory of Landsteiner and Levine. The reactions of the bloods of chimpanzees and monkeys with anti-M and anti-N sera can be explained most reasonably and simply by postulating the presence in these species of M-like and N-like agglutinogens rather than portions of a complicated gene complex; that is, the phenomena described are undoubtedly examples of the evolution of complicated chemical

molecules. Otherwise, it would be difficult to explain why the bloods of all chimpanzees tested possessed both M-like and N-like antigens. This must be due to a single agglutinogen having properties intermediate between M and N. If the reactions were due to separable antigens, M and N, then all chimpanzees would have to be heterozygous for M and N, which is not possible, because such an unstable distribution would be immediately upset by a single generation of random mating.

When we consider the A-B-O blood groups, the reasoning of Fisher and his co-workers leads to an even more confusing paradox. In place of gene A_1, we would have to substitute gene complex A_1AF_A; in place of gene A_2, the complex AOF_A; in place of gene B, the gene complex $B_iB_{ii}B_{iii}B_{iv}$; and in addition, there is the fourth possibility, gene O. So, instead of a series of four simple allelic genes, Fisher's logic leads us to a series of four nonhomologous chromosome segments of varying lengths. Again it would be difficult to explain why in the course of millions of tests no evidence has ever been obtained indicating crossing-over between these hypothetical gene complexes.

As I have pointed out before (A. S. Wiener and H. Karowe. *J. Immunol.*, 1944, 49, 51), a single letter should be used to designate agglutinogens behaving like units, and separate letters should be used only for agglutinogens that segregate genetically, e.g. group AB, type MN, type Rh_1Rh_2. To use a complicated designation like CDe for the unit agglutinogen Rh_1 is just as fallacious as to substitute the name type $M_iM_{ii}M_{iii}M_{iv}$ for the simple name type M. The pertinent question must now be raised as to whether in general, if a substance has several properties or characteristics, one must postulate a separate component to account for each characteristic. A cube has 6 faces, 12 edges, 8 vertices, 24 right angles, and so on, and the number of characteristics rapidly mounts as we amplify the description. Yet the cube, considered as a whole, is a unit. It seems to me that if Fisher's arguments were acceptable and carried to their logical conclusion, it would be necessary to scrap the entire gene theory.

In conclusion I should like to mention that almost everyone who has occasion to write on the Rh-Hr blood types seems to be impelled to propose another nomenclature, so that now more than six are extant. With regard to Fisher's designations, they have the disadvantages of being based upon an incorrect theory, of being unnecessarily complicated, of using symbols like *C*, *E*, and *e*, which have no relation to Rh and which have already been used in the field of blood grouping as symbols for other agglutinogens, and of including the symbol *d* for an agglutinogen the existence of which has not been demonstrated. The other nomenclatures suggested involve the use of numbers and therefore have the same objections as the Moss and Jansky numberings for the blood groups, with the addition that more permutations and combinations are possible, so that even greater confusion would result. Previous experience in the field of blood grouping has proved that progress will be furthered only by the universal use of a single, simple nomenclature. Since the symbolic designations of the Rh factors as Rh′, Rh″, and Rh_0, and of the Hr factors as Hr′ and Hr″, have proved to be the most logical, the simplest, and the least ambiguous, they should be universally adopted, also on the basis of priority.

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Consist—A Useful Noun

The language of America's railroad men suggests for English-speaking scientists a new noun—*consist*. The *consist* of a railroad train is more than the sum of the cars involved and is not just the route those cars take. A train may carry produce from Sunburst to Sweetgrass every day, but each time it will almost certainly have a new *consist*. The word includes in the content of its meaning not only the number and kind of cars—refrigerator cars, flat cars, or pullman cars—and all the necessary railroad identification, but also the arrangement of the cars according to destination and content. The cars are arranged so that in a train leaving Chicago the cars for Minneapolis can be dropped without detaching those destined for Grand Forks. Thus, within the meaning of *consist* there is the idea of possible subgroupings.

Biologically, the chromosome is a train of genes, and the *consist* of a given chromosome would be the chain of genes with the arrangement and kind of gene peculiar to a particular chromosome of a particular individual. Thus, every man has a Y-chromosome, and every Y-chromosome has certain features which distinguish it from the X-chromosome with which it is paired in a cell; furthermore, there are differences between the Y-chromosomes of various men. The *consist* of Charles Darwin's Y-chromosome was not the same as that of Jean Baptiste Lamarck's.

In the study of induced mutations where fragmentation of chromosomes occurs, the term *consist* seems to provide new conciseness to the discussion of results, for the *consist* of a chromosome would be altered no matter whether a fragment were altogether removed and destroyed, whether it were removed and attached elsewhere, or whether it were just removed, inverted, and reattached. The conventional language of gene loci relative to other genes becomes cumbersome in any dealing with these matters.

The chromosome, because of its linearity, provides an obvious application of the new noun, but it can also be applied without loss of meaning to three-dimensional bodies. The *consist* of a sodium chloride crystal would be sodium ions and chloride ions arranged alternately at the corners of cubes, eight of which in a large cube constitute the face-centered unit crystal of sodium chloride.

H. L. Mencken, in his *The American language* (Suppl. I), quotes Philip M. Wagner (*Amer. Speech*, 1940, 15, 342), who says that the origin of *consist* as a noun probably lies buried in the history of the papers with which the engineer of a train is provided before each run. These papers describe the cars of which his train consists, their arrangement in his train, and their destination along his route. The term is indeed sometimes applied

to these papers (*Life*, 1940, 8, No. 10, 55) and also sometimes by trainmen to the bill of fare of the diner (*Amer. Speech*, 1940, 15, 342).

To this writer the word was pronounced *con-sist'* by an American trainman, exactly like the verb.

There is no change in nomenclature suggested here but, rather, an amplification of the existing language. No redefining of words is necessary; but it might be suggested that there are already established alternatives.

Matrix is not a synonym of *consist*, because that word implies a skeleton which is to be filled in. *Consist* offers a more ample description than can be attained by simply using the word *locus*, for that word has a connotation of singularity. *Lattice* seems to suggest a too-specific kind of physical structure. *Group* is too vague and is lacking in a sense of spatial order.

Con-sist', then, is suggested as a noun, defined as the significant elements of which something is constituted together with all the relevant spatial arrangements of these elements.

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Book Reviews

Renal hypertension. **Eduardo Braun-Menéndez, Juan Carlos Fasciolo, Luis F. Leloir, Juan M. Muñoz, and Alberto C. Taquini. (Translated by Lewis Dexter.) Springfield, Ill.: Charles C. Thomas, 1946. Pp. xxx + 451. (Illustrated.) $6.75.**

When the solution of a problem as important as that of arterial hypertension has received an initial impetus by some outstanding contribution, the literature soon becomes filled with a mass of isolated, unrelated, and often conflicting observations. Gradually, as basic concepts begin to form, the various parts of the puzzle fall into place, and the gaps in knowledge become evident. In this book, a translation of *Hipertension arterial nefrogena* (Buenos Aires: Libreria y Editorial "El Ateneo," 1943), most of these observations are collected, edited, and presented in an orderly manner in an attempt to fit them to basic concepts and to demonstrate in what direction further work should proceed. Probably no other work on arterial hypertension has covered the field as well. The authors of the original work have made outstanding contributions to our knowledge of the subject, and are therefore as well qualified as any other group to write such a book. The translator, who has made a number of important contributions on the subject, has himself worked with the authors and is therefore best qualified not only to have made the translation but to have brought the English edition up to date.

The volume of material reviewed may be estimated in part by the number of references. In the original Spanish edition there were 1,104; in the English translation, 1,238. The title itself limits the material covered to the role of the kidneys in arterial hypertension, both experimental and clinical, and therefore perhaps insufficient attention is paid to the mechanism of hypertension produced experimentally by other methods, notably alterations in the nervous system and endocrine organs. However, these aspects of the problem are also well reviewed in an attempt to join them with known renal mechanisms. As a reference book for workers in the field this work is ideal. To the casual reader it might be somewhat confusing, but it gives as comprehensive a review of the subject as one can find in book form.

There are numerous illustrations, charts, and graphs, most of them taken from the authors' own works. It is fitting that the frontispiece is a drawing of Prof. B. A. Houssay, a pioneer on this problem, under whose direction and leadership much of this work was done. He writes a stimulating prologue, which is far too short.

Almost a third of the book is concerned with human arterial hypertension. This part may perhaps be criticized by those who are unwilling to accept the hypothesis that the kidneys play a predominant etiological role in human arterial hypertension. The conditions which are of most interest to medical scientists, namely, so-called "essential" hypertension and so-called "malignant" hypertension, are included under the heading, "Hypertension, Probably of Renal Origin" in the authors' classification of the syndrome, and are considered as such in the discussion on both medical and surgical treatment. This renal bias is justifiable until proof of the contrary is offered. (It is of passing interest that the word "possibly" is substituted for "probably" in the chapter heading for this aspect, in both the original and translated editions.) At any rate, the book offers strong suggestive evidence for many of the similarities between experimental renal hypertension and that type commonly found in man, *i.e.* "essential" hypertension, and as such represents a school of thought initiated by Goldblatt in 1934. The book ends with this statement: "The crucial proof of the identity of both would be the demonstration in the blood of the renal pressor substance responsible for the hypertension. This proof is still lacking. . . ." but there is no doubt how the authors really feel on the matter.

It is hoped that the translator will continue to keep the subject up to date in subsequent editions as he has so ably done in the present one.

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